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MARSHALL, GERSTEIN & BORUN LLP 233 SOUTH WACKER DRIVE 6300 SEARS TOWER CHICAGO, IL 60606-6357			FLOOD, MICHELE C	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

DETAILED ACTION

Acknowledgment is made of the receipt and entry of the amendment filed on September 21, 2009 with the addition of newly submitted Claims 84-87.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any rejection not repeated from the previous Office action mail dated April 1, 2009 is hereby withdrawn.

Claims 51-53 and 71-87 are under examination.

Response to Arguments

Claim Objections

Claims 71, 75, 79 and 83, as amended, are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claims, or amend the claims to place the claims in proper dependent form, or rewrite the claims in independent form. In the instant case, each of the claims recites a composition wherein the composition is claim-designated percentage amounts of claim-designated berries. However, the subject matter of independent Claims 51, 72 and 76 and 80 (from which the claims either directly or indirectly depend from comprise constituents of berries and not berries. Newly applied as necessitated by amendment.

Claim Rejections - 35 USC § 112

Claims 51-53 and 71-87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Newly applied as necessitated by amendment.

The metes and bounds of each of Claims 51 and 76 are rendered vague and indefinite by “wherein the composition has a higher antioxidant capacity than that of any one berry used in the composition” because this limitation is not commensurate in scope to the subject matter recited in the preamble of both claims. For instance, the preamble of each of the claims is drawn to a “composition comprising constituents [emphasized] of four or more berries” selected from a claim-designated Markush. A ‘constituent(s)’ is generally defined as a part of the whole of an entity. Therefore, the phrase, ‘constituents [emphasized] of four or more berries’, infers that the claimed composition comprises a part(s) or parts of berries and not any one (whole)berry itself. Since only “constituents of four more berries” comprise the instantly claimed compositions, no ‘one berry is used in the composition(s)’. The lack of clarity renders the subject matter to which Applicant seeks patent protection ambiguous.

With regard to Claims 52, 73, 77 and 81, the metes and bounds are rendered vague and indefinite for reasons similar to those set forth in the rejection immediately above. In the instant case, each of the claims recites “wherein the composition has a higher oxygen radical absorbance capacity than the oxygen radical absorbance capacity of any one berry used in the composition” because the claimed compositions

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do not comprise any 'one berry'. Instead, the claimed compositions comprise 'constituents of four or more berries'. The lack of clarity renders the subject matter to which Applicant seeks patent protection ambiguous.

All other cited claims depend directly or indirectly from rejected claims and are, therefore, also, rejected under U.S.C. 112, second paragraph for the reasons set forth above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 51-53, 72-74, 84 and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bomser et al. (U), Wedge et al. (V), Dufour et al. (N), Liu et al. (Liu, M et al., J. Agric Food Chem., April 4, 2002, 50: 2926-2930. Antioxidant and antiproliferative activities of raspberries.), Xue et al. (W) and Kandil et al. (X) in view of Prior et al. (U1), Wang et al. (V1) and Prior et al. (Prior, RL et al. Journal of AOAC International (2000), 83(4):950-956. Analysis of botanicals and dietary supplements for antioxidant capacity: A review.). Newly applied as necessitated by amendment.

Applicant claims a composition comprising constituents of four or more berries selected from the group consisting of blueberry, bilberry, cranberry, elderberry, and raspberry and strawberry, wherein the composition has a higher antioxidant capacity than that of any one berry used in the composition. Applicant further claims the composition of claim 51, wherein the composition has a higher oxygen radical absorbance capacity than the oxygen radical absorbance capacity of any one berry extract used in the composition; wherein the composition has an oxygen radical capacity above 40 Trolox equivalents/gram fresh weight basis; and, wherein the berries are blueberry, bilberry, raspberry and strawberry. Applicant further claims the composition of claim 72, wherein the composition has a higher oxygen radical absorbance capacity than the oxygen radical absorbance capacity of any one berry extract used in the composition; and, wherein the composition has an oxygen radical capacity above 40 Trolox equivalents/gram fresh weight basis. Applicant further claims the composition of claim 51, wherein the constituents are selected from the group consisting of polyphenols, flavonoids, anthocyanins, or mixtures thereof. Applicant

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further claims the composition of claim 84, wherein polyphenols comprise ferulic acid, catechin, rutin, and mixtures thereof.

Bomser beneficially teaches, "Fruit extracts of four *Vaccinium* species (lowbush blueberry, bilberry, cranberry, and lingonberry) were screened for anticarcinogenic compounds by a combination of fractionation and in vitro testing of their ability to induce the Phase II xenobiotic detoxification enzyme quinone reductase (QR) and to inhibit the induction of ornithine decarboxylase (ODC), the rate-limiting enzyme in polyamine synthesis, by the tumor promoter phorbol 12-myristate 13-acetate (TPA). The crude extracts, anthocyanin and proanthocyanidin fractions were not highly active in QR induction whereas the ethyl acetate extracts were active QR inducers. The concentrations required to double QR activity (designated CD_{qr}) for the ethyl acetate extracts of lowbush blueberry, cranberry, lingonberry, and bilberry were 4.2, 3.7, 1.3, and 1.0 microgram tannic acid equivalents (TAE), respectively, Further fractionation of the bilberry ethyl acetate extract revealed that the majority of inducer potency was contained in a hexane/chloroform subfraction (CD_{qr} = 0.07 microgram TAE). In contrast to their effects on QR, crude extracts of lowbush blueberry, cranberry, and lingonberry were active inhibitors of ODC activity. The concentrations of these crude extracts needed to inhibit ODC activity by 50% (designated IC₅₀) were 8.0, 7.0, and 9.0 micrograms TAE, respectively. The greatest activity in these extracts appeared to be contained in the polymeric proanthocyanidin fractions of the lowbush blueberry, cranberry, and lingonberry fruits (IC₅₀ = 3.0, 6.0, and 5.0 micrograms TAE, respectively). The anthocyanidin and ethyl acetate extracts of the four *Vaccinium*

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species were either inactive or relatively weak inhibitors of ODC activity. Thus, components of the hexane/chloroform fraction of bilberry and of the proanthocyanidin fraction of lowbush blueberry, cranberry, and lingonberry exhibit potential anticarcinogenic activity as evaluated by in vitro screening tests.”

In another instance, Wedge beneficially teaches, “Freeze-dried fruits of two strawberry cultivars, Sweet Charlie and Carlsbad, and two blueberry cultivars, Tifblue and Premier were sequentially extracted with hexane, 50% hexane/ethyl acetate, ethyl acetate, ethanol, and 70% acetone/water at ambient temperature. Each extract was tested separately for in vitro anticancer activity on cervical and breast cancer cell lines. Ethanol extracts from all four fruits strongly inhibited CaSki and SiHa cervical cancer cell lines and MCF-7 and T47-D breast cancer cell lines. An unfractionated aqueous extract of raspberry and the ethanol extract of Premier blueberry significantly inhibited mutagenesis by both direct-acting and metabolically activated carcinogens.”

Dufour beneficially teaches a composition comprising an anthocyanoside-containing extract derived from the fruit of bilberry, which is used to prevent cancer proliferation in the intestines and colon. Dufour further teaches that the anthocyanosides of the bilberry extract have antioxidant and anti-free radical actions and are not digested in the small intestines but rather assimilated in the terminal part of the colon) and also restores the microbial balance in the intestine by increasing the population of bifidogenic bacteria (resulting in reduction in intestinal pH).

Liu beneficially teaches raspberry extracts rich in anthocyanins and having high antioxidant activity and antiproliferative activity against human cancer cells in a dose-

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dependent manner. The antioxidant activity of the raspberry was directly related to the total amount of the phenolics and flavonoids found in the raspberry. In Figure 2, Liu illustrates the antioxidant activity of four extracts obtained from four different cultivars of raspberries.

Xue beneficially teaches various fractions of raspberry and strawberry extracts comprising having the ability to inhibit morphological cell transformation in cells treated with B[a]P (benzo[a]pyrene). Extracts comprising ellagic acid, as well as extracts not comprising ellagic acid, exerted chemopreventive activity. Xue concludes, "These results suggest that a methanol extract from strawberries and black raspberries may display chemopreventive activity. The possible mechanism by which these methanol fractions (FA-ME, RU-ME) inhibited cell transformation appear to involve interference of uptake, activation, detoxification of B[a]P and/or intervention of DNA binding and DNA repair." Xue further reports that in a study conducted by Stoner et al., freeze-dried strawberry when feed as five or ten percent of the diet, inhibited the development of esophageal cancer.

Kandil beneficially teaches, "Phenolics from the American cranberry (*Vaccinium macrocarpon*) were fractionated into a series of proanthocyanidins and other flavonoid compounds by vacuum chromatography on a hydrophilic, porous polyvinyl gel permeation polymer. Antioxidant activity was not restricted to a particular class of components in the extract but was found in a wide range of the fractions. Significant chemopreventive activity, as indicated by an ornithine decarboxylase assay, was localized in one particular proanthocyanidin-rich fraction from the initial fractionation

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procedure. Further fractionation of the active anticarcinogenic fraction revealed the following components: seven flavonoids, mainly quercetin, myricetin, the corresponding 3-O-glycosides, (-)-epicatechin, (+)-catechin, and dimers of both gallocatechin and epigallocatechin types, and a series of oligomeric proanthocyanidins.” See abstract. Kandil further teaches that the berry fractions have antioxidant capacity.

The individual teachings of Bomser, Wedge, Dufour, Liu, Xue and Kandil, as set forth immediately, teach that it was known in the art at the time of the invention that each of the claim-designated berries of blueberry, bilberry, cranberry, raspberry and strawberry was known in the art to contain polyphenols, to exert radical scavenging, anti-oxidative, and anti-cancer activities. None of the references teach a composition comprising constituents of each of the claim-designated berries. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the claim-designated ingredients in the making of the claimed composition because it is well known that its *prima facie* obvious to combine two or more ingredients each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is useful for the same purpose. The idea for combining them flows logically from their having been used individually in the prior art. *In re Pinten*, 459 F. 2d 1053, 173 USPQ 801 (CCPA 1972); *In re Susi*, 58 CCPA 1074, 1079-80; 440 F.2d 442, 445; 169 USPQ 423, 426 (1971); *In re Crockett*, 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960).

The combined references do not specifically teach a composition wherein the composition has a higher antioxidant capacity than that of any one berry used in the

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extract or wherein the composition has a higher oxygen radical absorbance capacity than the oxygen radical absorbance capacity of any one berry used in the extract, or wherein the composition has an oxygen radical absorbance capacity above 40 Trolox equivalents/gram fresh weight basis. Prior (U1) teaches that the Trolox equivalent antioxidant capacity of blueberry extracts (*Vaccinium* L.), as measured by ORAC, ranged from a low of 13.9 to 45.9 micromole TE/g of fresh berries, depending upon the maturity, the anthocyanin and total phenolic content and variety of the blueberry. See Table 1. Prior further teaches, "Bilberry and the lowbush blueberry blueberries (as taught by Bomser) from Nova Scotia had the highest antioxidant capacity (44.6 +/- 2.3 and 45.9 +/- 2.2, respectively) as well as total phenolics 525 +/- 5.0 and 495 +/- 3.5, respectively) (Table 2). There appear to be clusters of ORAC values in the lowbush blueberries. The first include lowbush-PEI, lowbush-NS, and Fundy lowbush blueberries (Table 2) which were relatively high in ORAC (mean: 41.8), anthocyanins, and total phenolics. The second cluster included lowbush from ME (Table 1), cv. Cumberland, and cv. Blomidon (Table 2) lowbush blueberries which were lower in ORAC (mean: 27.5)." On page 2878, second Column, first paragraph, Prior teaches that the bilberries included in the study represented a mixture of wild clones. Prior further teaches ORAC value of late harvest Tifblue (blueberry rabbiteye cultivar), as taught by Wedge, has a ORAC value of 37.8. See page 2588, Column 2, lines 5-20; Table 1 and Table 2. Wang teaches that, on the basis of wet weight (edible portion) that strawberry had a relatively high antioxidant capacity of 15.4 μ mol Trolox equivalents (TE)/g of fresh weight. In Table I, Wang also (V1) measured the antioxidant capacity of strawberry fruit

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extract (such as the strawberry extracts taught by Wedge) using the oxygen radical absorbance capacity (ORAC) assay with regard to the effect of acetone extraction time on ORAC (nanomoles of Trolox equivalents per gram) measured in fruit pulp, wherein the TEAC/g ranged from 847 ± 29 (2 min) to 1129 ± 113 (4h). In another instance, Prior (2000) teaches that strawberries, blueberries, cranberries and raspberries have an antioxidant capacity greater than 100, on page 951, last paragraph. Given the teachings as a whole, the artisan of ordinary skill made have had a reasonable expectation that the combining of the ingredients taught by the references as disclosed by Applicant would be a success in providing not only a composition having a higher antioxidant capacity than any one berry extract used in the composition and a higher oxygen radical absorbance capacity than the oxygen radical absorbance capacity than one berry extract used in the composition, but would also be a success in the making of a dietary supplement capable of mitigating the effects of oxidative stress implicated in the pathogenesis of cancer, as well as heart disease. This reasonable expectation of success would have motivated the artisan of ordinary skill to combine the instantly claimed ingredient, especially given the teachings of Prior (For example, on page 2692, last paragraph of Column 2, Prior teaches, "Studies are continuing in our laboratory of the implications of consuming foods containing increased quantities of ORAC. The antioxidant rich phytochemicals in strawberries have been shown in rat models to reduce or retard the central nervous system deficits seen in aging [citation omitted] and to protect against the oxidative stress caused by 100% oxygen exposure [citation omitted]. Since the antioxidant capacity of blueberries is higher than for strawberries, a

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benefit of consuming antioxidants from blueberries would also be expected.

Furthermore, consumption of a more concentrated source of antioxidants will have the greatest impact on in vivo antioxidant capacity. We have estimated that normal intake in humans of antioxidants as measured by ORAC within the U.S. is in the range of 1.2-1.7 mmol ORAC/day [citation omitted]. Increases in serum ORAC are observed with intakes of 3-4 mmol Trolox equiv/day, and some individuals have been observed to have ORAC intakes as high as 6 mmol/day [citation omitted]. Consumption of ½ cup of blueberries (72.5) would increase ORAC intake by 1-3.2 mmol, depending upon the blueberry variety and maturity. Thus, the ORAC of the blueberry source can have marked effects of total daily ORAC intake.” Thus, at the time the invention was one of ordinary skill in the art would have been motivated and one would have had a reasonable expectation of success to combine constituents of four or more of the berries taught by the combined references to provide the instantly claimed composition because the claimed invention is no more than the combining of well known ingredients known for their beneficial functional effect to mitigate the effects of free radicals due to their high oxygen radical absorbance capacities and in general beneficial to health and contributing to the proliferation and development of cancer.

Based upon the beneficial teachings of the cited references, the skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Accordingly, the claimed invention was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence

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to the contrary.

Claims 76-78, 80-82, 86 and 87, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over Bomser et al. (U), Wedge et al. (V), Dufour et al. (N), Liu et al. (Liu, M et al., J. Agric Food Chem., April 4, 2002, 50: 2926-2930. Antioxidant and antiproliferative activities of raspberries.), Xue et al. (W) and Kandil et al. (X) in view of Prior et al. (U1), Wang et al. (V1) and Prior et al. (Prior, RL et al. Journal of AOAC International (2000), 83(4):950-956. Analysis of botanicals and dietary supplements for antioxidant capacity: A review.), and further in view of Moyer et al. (W1). Newly applied as necessitated by amendment.

Applicant claims a composition comprising constituents of four or more berries selected from the group consisting of wild blueberry, wild bilberry, cranberry, elderberry, raspberry and strawberry, wherein the composition has a higher antioxidant capacity than that of any one berry used in the composition. Applicant further claims the composition of claim 76, wherein the berries are wild blueberry, wild bilberry, raspberry and strawberry. Applicant further claims the composition of claim 80, wherein the composition has a higher oxygen radical absorbance capacity than the oxygen radical absorbance capacity of any one berry extract used in the composition; and, wherein the composition has an oxygen radical capacity above 40 Trolox equivalents/gram fresh weight basis. Applicant further claims the composition of claim 76, wherein the composition has a higher oxygen radical absorbance capacity than the oxygen radical

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absorbance capacity of any one berry extract used in the composition; and, wherein the composition has an oxygen radical capacity above 40 Trolox equivalents/gram fresh weight basis. Applicant further claims the composition of claim 76, wherein the constituents are selected from the group consisting of polyphenols, flavonoids, anthocyanins, or mixtures thereof. Applicant further claims the composition of claim 86, wherein polyphenols comprise ferulic acid, catechin, rutin, and mixtures thereof.

The combined teachings of Bomser, Wedge, Dufour, Liu, Xue and Kandil per the teaching of Xue, Kandil, Prior and Wang, as set forth above, teach the instantly claimed invention except for wherein one of the berries is a wild berry.

Moyer teaches the total anthocyanins and total phenolic contents and antioxidant capacities as determined by oxygen radical absorbing capacity (ORAC) of fruits of various blueberries (*Vaccinium* L.) in Table 1. Moyer teaches that both blueberry extract and wild blueberry extract have high ORAC values in terms of Trolox equivalents micromoles per gram on fresh weight basis, as well as high contents of anthocyanins and phenolics. Thus, it was known in the art at the time of the invention, that both blueberry extract and wild blueberry extract have high antioxidant capacity as measured by an oxygen radical absorbance capacity assay; and that the highest ORAC values observed in the blueberry (*Vaccinium* L.) population belonged to wild blueberry extract. For example, wild selections of rabbiteye blueberry, *Vaccinium ashei*, from Florida and Georgia had the highest ORAC (131, 129 and 122/ $\mu\text{mol TE/g}$. See Table 1. Therefore, an artisan of ordinary skill would have had a reasonable expectation that using wild blueberry or blueberry having relatively high ORAC values would be useful in preparing

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a composition having the claim-designated physical parameters when combined with any of the constituents of one or more of the berries comprising the composition taught by the combined teachings of Bomser, Wedge, Dufour, Liu, Xue and Kandil. This reasonable expectation of success would have motivated the artisan to add the wild blueberry as taught by Moyer to the composition taught by the combined teachings of Bomser, Wedge, Dufour, Liu, Xue and Kandil to provide the instantly claimed composition, especially since it was well established that blueberry extracts having high antioxidant capacity and high contents of anthocyanins and phenolics are beneficial in the making of dietary supplements due to their health promoting effects; and could augment the beneficial health promoting effects of the strawberry based products, as discussed by Prior.

Based upon the beneficial teachings of the cited references, the skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Accordingly, the claimed invention was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELE FLOOD whose telephone number is (571)272-0964. The examiner can normally be reached on 7:00 am - 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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